CASE REPORT

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From shortness of breath to diagnosis of Burkitt lymphoma – a case of an 8-year-old paediatric patient

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Abstract

Burkitt lymphoma (BL) is an aggressive B-cell cancer In children usually located in the abdomen. The case is presented of an 8-year-old boy with aggressive disseminated BL involving the liver, lungs, kidneys, intestines, pleura, and bone marrow. The patient was admitted to the emergency department due to worsening shortness of breath and cough, which had persisted for a week despite treatment. An ultrasound and CT scan were performed, which revealed liver enlargement, fluid in the abdomen and pleura, and multiple tumour foci. During the course of the disease, tumour lysis syndrome developed. Treatment with glucocorticosteroids and chemotherapy was initiated, which led to significant regression of the liver lesions. After 2 months, follow-up examinations showed disease progression and the appearance of new lesions in the chest. The case highlights the importance of ultrasound in children with suspected cancer, and the role of recognizing characteristic imaging features of BL for rapid diagnosis.

Key words

ultrasonography, tumour lysis syndrome, chemotherapy, Burkitt lymphoma, lymphoma in children

INTRODUCTION

Burkitt lymphoma (BL) is an aggressive B-cell cancer associated with EBV, HIV, and chromosomal translocations [1]. In children, it is usually located in the abdomen, affecting the intestines, lymph nodes, or retroperitoneal space. BL is an aggressive cancer with high growth dynamics, whose clinical symptoms can be very diverse. Due to the rapid proliferation of the cancer cells, it can cause symptoms resulting from pressure on internal organs or intestinal involvement [2]. The case is presented of an 8-year-old boy with aggressive disseminated Burkitt lymphoma involving, among others, the liver, lungs, kidneys, intestines, pleura, and bone marrow, which, despite initial improvement after treatment, showed rapid disease progression leading to death.

CASE REPORT

An 8-year-old boy was admitted to the Emergency Department due to worsening shortness of breath and coughing which had persisted for a week, despite inhalation treatment. An abdominal ultrasound was performed which showed enlargement of the liver with focal lesions, and the presence of free fluid in the lower abdomen. (Fig. 1 A-B). The patient was referred to the Department of Paediatric Haematology, Oncology, and Transplantology, where subsequent CT scans confirmed liver enlargement with numerous hypodense foci, and showed the presence of infiltrates in the intestines and kidneys (Fig. 1 C-D). A CT scan of the chest revealed numerous irregular areas of parenchymal thickening in the right lung, the presence of fluid in the pleural cavity, and pathological tumour infiltration in the subpleural area (Fig. 1 E-H). Due to the patient's severe condition, a biopsy of the abdominal tumour was not performed. After imaging, the patient was transported to the operating theatre for pleural cavity puncture, bone marrow aspiration biopsy, and Broviac catheter implantation. Shortly thereafter, the patient was transferred to the Intensive Care Unit due to electrolyte disturbances caused by tumour lysis syndrome. During treatment, electrolyte disturbances were corrected (hyperkalaemia, hypocalcaemia, hyperphosphataemia, hypermagnesaemia, and hyperuricaemia). An insulin–glucose infusion was administered, inhaled salbutamol was used, calcium supplementation provided, and acid–base disturbances corrected with sodium bicarbonate ($NaHCO_3$). Due to the patient's severe condition, analgosedation was initiated using ketamine, morphine, and thiopental. On day 17 of treatment, the patient spontaneously opened his eyes and reached for the endotracheal tube; therefore, analgosedation was reduced. On day 19 of treatment, the boy was conscious, in logical contact; speech was difficult and quiet. On day 21 of treatment, the patient was transferred from the Intensive Care Unit back to the Department of Paediatric Haematology, Oncology, and Transplantology. Based on the pathological examination, the patient was diagnosed with Burkitt's lymphoma. Treatment with R-CHOP protocol (rituximab, cyclophosphamide, doxorubicin, vincristine and methylprednisolone) was initiated, which led to significant regression of the liver lesions.

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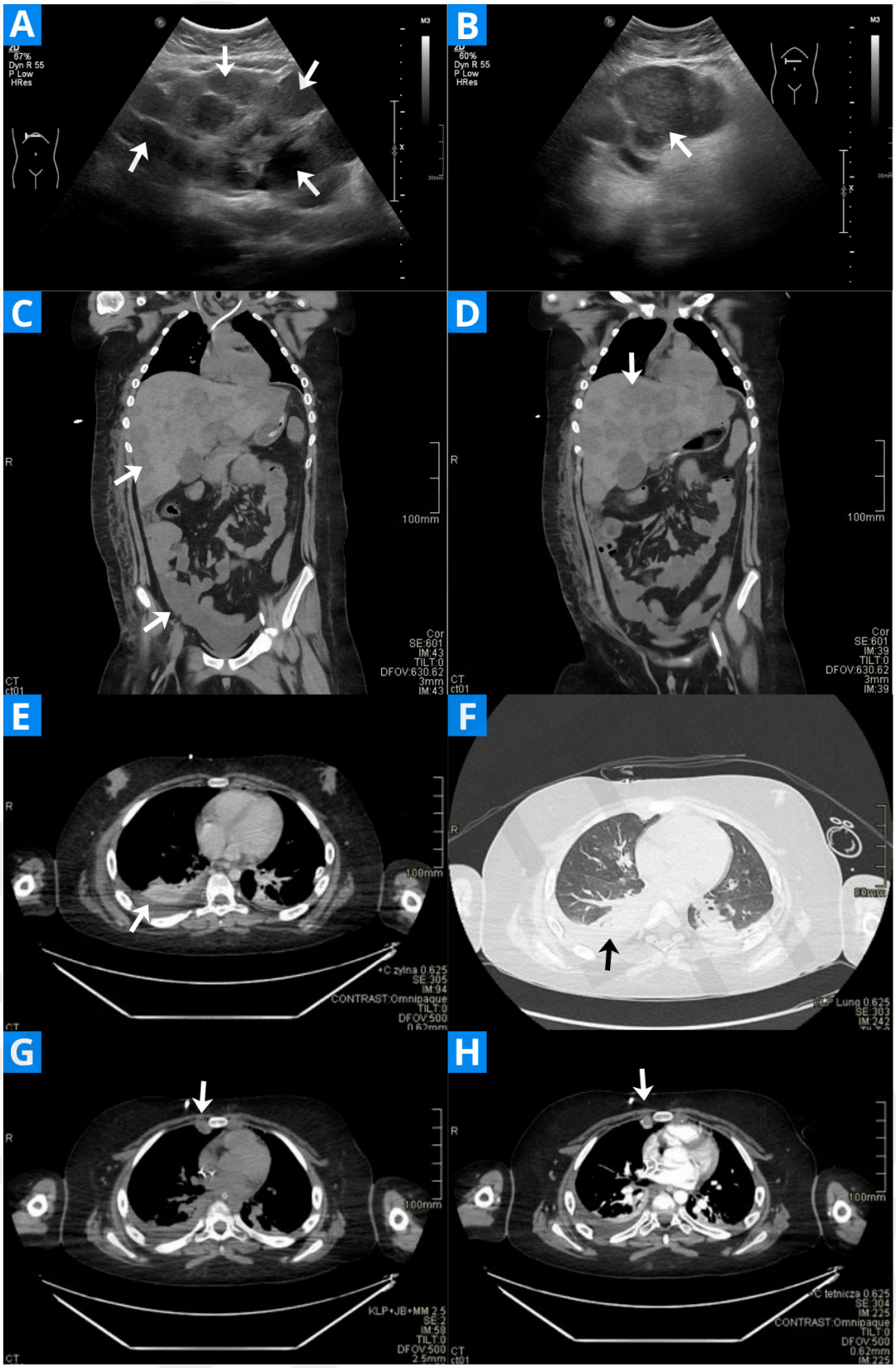

Figure 1. (A-H). Ultrasound examination revealed an enlarged, heterogeneous liver with numerous focal lesions occupying most of the liver parenchyma (A), the largest of which was located in the left lobe and measured approximately 65 mm in diameter (B). The remaining liver parenchyma showed increased echogenicity, indicating signs of steatosis. A CT scan revealed fatty tissue erosion in the right paracolic gutter area and subcutaneous tissue oedema covering the chest (C), as well as fluid in the abdominal cavity and pelvis and numerous metastatic lesions in the liver (D). A chest CT scan revealed numerous irregular areas of pulmonary parenchymal consolidation, most pronounced in the dorsal segments, especially in the right lung, and extensive, irregular areas of ground-glass opacity in both lungs. Fluid in the right pleural cavity with a thickness of up to 14 mm and in the interlobar fissure (E,F). An oval area measuring approximately 14x16x25 mm (APxRLxCC) is visible in the right paracardiac subpleural space, with an average density of approximately 16 HU, with marginal enhancement after administration of a meta-type contrast agent (G,H).

After 2 months, follow-up examinations (PET-CT, CT, and ultrasound) showed disease progression and the appearance of new lesions in the chest. PET showed significant progression of pathological changes with high glucose uptake, involving the pleura, especially on the right side, with partial involvement of the left side, chest lymph nodes, infiltrative lesions in the right lung, extensive involvement of the abdominal cavity (including the liver, mesentery, paracolic grooves, and chest wall), as well as bone marrow involvement. Due to disease progression, a new oncological treatment was initiated as part of the R-VICI protocol (rituximab, vincristine, ifosfamide, cyclophosphamide, idarubicin). Following 3 months, in the setting of massive disease progression, failure of previous therapy, and a very poor prognosis, third-line therapeutic options were discussed, including palliative treatment with glofitamab and obinutuzumab. The patient died due to metastatic cancer, which secondarily led to multi-organ failure.

DISCUSSION

The importance of imaging studies in patients with suspicion of Burkitt's lymphoma has long been a continuous issue. As early as 1985, radiologists were relying on ultrasound as one of the primary diagnostic tools for children with abdominal tumours [3]. Nevertheless, the ultrasonographic presentation of abdominal Burkitt's lymphoma has not been consistent.

The most commonly affected areas in the abdominal region are the ileum and caecum, as these areas have a higher percentage of lymphatic tissue than other gastrointestinal regions [4]. Therefore, one of the most frequent seen pathologies are enlarged lymph nodes. Moreover, lesions in soft tissues appearing as tumours are also evident on the ultrasonography [5]. Ultrasonographic findings such as intussusception may also indicate Burkitt's lymphoma, as lymphomas are the most common neoplastic etiology of this pathology [4, 6]. The intussusception is visible as a 'target sign' lesion and 'pseudokidney' sign [4]. The addition of Doppler can show vascular flow disturbance around the layers of the intussusception.

Even though ultrasound (US) is often the first imaging technique used to assess palpable abdominal masses, computed tomography (CT) plays a crucial role in determining the extent and severity of the disease for accurate tumour staging [4]. Burkitt lymphoma (BL) involving the bowel can present either as a localized mass or as a segment of thickened bowel wall, which is often described as aneurysmal in appearance and may be accompanied by dilation of the intestinal lumen. When a mass connects with the bowel lumen, pockets of internal air may be seen. CT imaging shows the characteristic telescoping of one bowel segment into another, along with the dragged-in mesenteric fat and vessels. It also provides a clearer view of the severity and reach of any upstream bowel obstruction [4]. In the presented patient, in the area of the small intestine below the tail of the pancreas, an irregular, poorly defined round area was visible, with a slight enhancement at the margins after contrast administration. A CT scan with contrast of the patient's abdomen also revealed an enlarged liver with numerous round hypodense focal lesions modelling the contours of the liver capsule, suggesting infiltrative changes in the course of the underlying disease.

On the contrary, magnetic resonance imaging characteristics of Burkitt lymphoma in pediatric patients are not well documented in the existing literature. A contrast-enhanced head MRI scan performed on the presented patient revealed marked, small hyperintense areas within the periventricular white matter on Dark Fluid and T2W images directly adjacent to the frontal horns and lateral ventricles, which were non-specific in nature. CT and MRI imaging assist in assessing the metastases to surrounding structures. MRI is superior for assessing soft tissue and bone marrow involvement, offering superior soft tissue contrast that can better reveal tumour spread. CT is more effective in detecting bone destruction, however, it offers limited soft tissue contrast and involves exposure to ionizing radiation. Since MRI does not use ionizing radiation, it is generally safer for paediatric patients [7]. Despite these advantages, MRI has certain drawbacks compared to CT, including longer examination times and reduced availability, especially in emergency situations [4]. Additionally, children are much more likely to require sedation, which is undesirable when there is a risk of airway obstruction [8].

The clinical presentation of Burkitt's lymphoma is variable depending on the area of the body involved. Abdominal involvement is often associated with abdominal pain or distension [9].

The main concern for the patient during the first doctor visit was shortness of breath associated primarily with pulmonary problems, and is a symptom that may occur with excessive pressure from the tumour mass. Additionally, the high incidence of patients with BL, experience life-threatening conditions called tumour lysis syndrome [10, 11], a potentially alarming complication that can be induced by prolonged fever or the administration of anaesthetics, which may also have contributed to TLS in the presented patient [11].

As stated in one of the retrospective analysis on 570 patients, tumour lysis syndrome can be the cause of death even in 11.9% cases in patients with Burkitt's lymphoma [12]. The appearance of symptoms such as ventricular tachycardia with wide QRS complexes, electrolyte disturbances, and hypotension in the presented patient during pleural cavity puncture, bone marrow biopsy, and Broviac catheter placement, indicated the development of TLS. As these procedures may trigger TLS, it is vital to administer pre-operative hydration and hypouricemic agents [11]. With asymptomatic onset, patients may then experience nausea, vomiting, seizures, apathy, hydrops or cardiac dysrhythmias [13]. During the hospital admission of the presented patient, the laboratory tests revealed electrolyte imbalances – hyperkalaemia. Simultaneously, heart arrhythmia – ventricular tachycardia was also observed. Patients diagnosed with intussusception also present with chronic abdominal pain and concerning blood results [14]. Acute abdominal pain is often considered to be the clinical presentation of acute appendicitis, and a diagnosis of Burkitt lymphoma is rarely the first to be made [5, 15]. Such patients may not experience the most common symptoms of lymphoma, but may experience vomiting or nausea. There are also situations in which patients have two coexisting disorders (e.g. Burkitt's lymphoma and Meckel's diverticulum), which makes diagnosis more complex [14]. At the same time, a prompt diagnosis of the neoplastic process, Burkitt's lymphoma is key to the outcome of the patient.

However, the optimal standard of care for Burkitt lymphoma has yet to be clearly established. Rapid initiation

of therapy, preferably within 48 hours of diagnosis, is essential [16]. Two frequently used therapeutic approaches for Burkitt lymphoma include the dose-adjusted EPOCH-R and EPOCH-RR regimens. These protocols combine etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin with rituximab. Treatment selection and intensity are tailored according to whether the disease is classified as low- or high-risk [17]. Other chemotherapy guidelines that emphasize multiagent treatment strategies along with central nervous system prophylaxis, recommended by The National Comprehensive Cancer Network are: R-hyper-CVAD, CODOX-M/IVAC with or without the addition of rituximab, and dose-adjusted EPOCH combined with rituximab [16]. Immunotherapy also has an important role in the of management of Burkitt lymphoma. Rituximab, an anti-CD20 monoclonal antibody, is recommended as part of all treatment protocols because its use is associated with improved outcomes [16]. Chemotherapy combined with rituximab can improve the prognosis of children with stage III/IV BL [18]. Also the incorporation of rituximab into the modified BFM-NHL-95 chemotherapy protocol significantly improved outcomes for children and adolescents with BL in risk groups R2 through R4 [19]. Newer anti-CD20 antibodies, including ofatumumab and obinutuzumab, are currently being studied. Additional agents under investigation include blinatumomab, which targets CD19, and inotuzumab, which targets CD22. Therapeutic strategies aimed at inhibiting the MYC oncogene are also under active investigation [16]. Although the prognosis for this disease is excellent in children undergoing intensive chemotherapy [16], in the case of the presented patient, first- and second-line treatments were unsuccessful. For this reason, third-line treatment was used, including palliative treatment with glofitamab and obinutuzumab.

Monitoring oncology patients after first-line treatment is an indispensable stage of treatment, as according to clinical studies, 6.4%, 10%, and up to even 15.2% of patients, may experience disease relapse [20, 21]. The prognosis for these patients is unfavourable, although with salvage therapy, autologous stem cell transplants, and the increased introduction of CART therapy, PFS results are improving [22].

CONCLUSIONS

Despite atypical symptoms such as dyspnoea or gastrointestinal bleeding, an abdominal ultrasound examination should be routinely performed for patients suspected of having malignancy. At the same time, recognizing the typical imaging features and common sites of involvement facilitates prompt detection and accurate diagnosis of Burkitt lymphoma. The examination should not only focus on the lookout of the hypoechoic lesions, but also intussusception and thickening of the bowel walls.

These measures may facilitate earlier detection of the disease at an early stage and, consequently, allow for the prompt initiation of treatment. As a result, the chances of the patient achieving remission more rapidly and prolonging survival are improved. Diagnosis of Burkitt's lymphoma is only the beginning of the strict monitoring of patients for urgent states such as tumour lysis syndrome.

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